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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,654	03/29/2001	Kenichi Hosoya	10939/2012	6149

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PALMER & DODGE, LLP
PAULA CAMPBELL EVANS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/821,654	HOSOYA ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is a response to the Paper filed 7 February 2005 in reply to the Final Office Action mailed 28 December 2004. Finality of the previous Office Action is hereby **withdrawn** in view of the new grounds for rejection set forth herein below. Claims 1-14 were previously considered. Claims 1-14 are presently pending and under consideration.

Response to Amendment

Claim Rejections - 35 USC § 102

Rejection of claims 1-6 under stand rejected 35 U.S.C. 102(a) as being anticipated by Hosoya et al., claims 7-10 under 35 U.S.C. 102(a) as being anticipated by Kitazawa et al. and claims 11-14 under 102(a) as being anticipated by Hosoya et al. is withdrawn in view of the filing of the required priority documents.

New Grounds

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 11, 12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Jat *et al.* (1997) US Patent No. 5,688,692 as evidenced by Greenwood *et al.* (1996) *J. Neuroimmunol.* 71:51-63.

Claims 1-4, 6, 11, 12 and 14 are directed to a conditionally immortalized cell established from a transgenic animal into which a large T-antigen gene of SV40 temperature sensitive mutant tsA85 has been introduced, wherein the cells express various phenotypic characteristics which are disclosed as inherent to capillary endothelial cells established from brain or choroid plexus (see especially the discussion bridging pages 44-45 of the specification). The claims also require that the cells do not contain a heterologous antibiotic resistance gene. Please note that, although the claims recite process steps, a product-by-process claim reads on the claimed cells made by any means. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) states: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Jat *et al.* teaches production of a transgenic mouse comprising a transgene comprising a tsA85 mutant of SV40 large T-antigen, wherein all vector sequences were removed from the transgene prior to introducing into fertilized mouse eggs such that the cells of the transgenic mouse do not comprise a heterologous antibiotic resistance gene (see especially the first full paragraph in column 16). Jat *et al.* further teaches establishing a culture of brain capillary endothelial cells from the transgenic animal (see Example 6, beginning in column 26), which brain capillary endothelial cells are the same as the cells of claim 1 and brain capillary endothelial cells of the instant claims 11, 12 and 14. Furthermore, as Greenwood *et al.* teaches that retinal and brain vascular endothelial cells are believed to be identical, the brain vascular

endothelial cells of Jat *et al.* also anticipate the retinal capillary endothelial cells of claims 2, 3, 4 and 6.

The conditionally immortalized cell of Jat *et al.* is the same as the cell of the instant claims; therefore, the claims are anticipated by Jat *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jat *et al.* (*supra*).

The claim is directed to a method for establishing a conditionally immortalized cell comprising treating brain capillary vessels of a transgenic animal into which a large T-antigen of SV40 mutant tsA58 has been introduced with protease, subculturing the resulting cells at 33 °C, and identifying said conditionally immortalized cell.

Jat *et al.* teaches a method for establishing a conditionally immortalized cell comprising treating brain capillary vessels of a transgenic animal into which a large T-antigen of SV40 mutant tsA58 has been introduced with colagenase:dispase and subculturing the resulting cells (see Example 6, beginning in column 26). Although Jat *et al.* does not explicitly teach that the capillary endothelial cells were subcultured at 33 °C, this limitation would be obvious to one of ordinary skill in the art at the time of filing because Jat *et al.* identifies 33 °C as the permissive temperature for expression of the tsA58 transformed phenotype (see, *e.g.*, column 14, lines 21 and 35; column 18, lines 14, 27, 35 and 44; column 19, line 14; column 22, line 20; column 23, line 64; column 5, line 57; and column 29, line 9). These teachings provide direction and reasonable expectation of success, and one would be motivated to grow the cultures at 33 °C in order to immortalize the cells, which is the nature of the problem solved in the method of Jat *et al.*

For these reasons, the method of claim 13, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenwood *et al.* (*supra*) in view of Jat *et al.* (*supra*).

Again, the product claims 1-4, 6, 7, 8, 10-12 and 14 are product-by-process claims and, as such, read on the product made by any process. Thus, the claims are directed to cells having the features recited in the claims made by any means.

Claim 5 is directed to a method for establishing a conditionally immortalized cell comprising treating retinal capillary vessels of a transgenic animal into which a large T-antigen of SV40 mutant tsA58 has been introduced with protease, subculturing the resulting cells at 33 °C, and identifying said conditionally immortalized cell, and claim 9 is directed to a method for establishing a conditionally immortalized cell comprising treating choroidal epithelium of a transgenic animal into which a large T-antigen of SV40 mutant tsA58 has been introduced with protease, subculturing the resulting cells at 33 °C, and identifying said conditionally immortalized cell.

Greenwood *et al.* teaches a method for establishing a conditionally immortalized retinal endothelial cell or retinal pigment epithelial cell comprising treating retinal capillaries or choroidal epithelial cells with protease and culturing the cells (see especially the second and third paragraphs on page 53). Greenwood *et al.* further teaches transforming the cells by introducing an SV40 tsA58 gene. Greenwood *et al.* does not teach establishing cells from a transgenic animal into which a large T-antigen gene of SV40 temperature sensitive mutant tsA58 has been introduced or growing the cells at 33 °C.

As described above, Jat *et al.* teaches production of a transgenic mouse comprising a transgene comprising a tsA85 mutant of SV40 large T-antigen, wherein all vector sequences

were removed from the transgene prior to introducing into fertilized mouse eggs such that the cells of the transgenic mouse do not comprise a heterologous antibiotic resistance gene. Jat *et al.* further teaches establishing cultures of a wide variety of cell types from the transgenic animal (see Examples 1-9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of establishing the retinal endothelial or retinal pigment epithelial cell lines of Greenwood *et al.* to include establishing the lines from the transgenic animal of Jat *et al.* in accordance with the limitations of the instant method claims and to produce the cells of the instant product claims. Motivation to modify the teachings comes from Jat *et al.*, who teaches in column 2:

> Various types of transfection strategies exist, and retroviral-mediated gene insertion is the most commonly used strategy for introducing immortalizing genetic elements. These strategies share a number of disadvantages. First, there is at present no means of targeting specific cellular populations. Second, the efficiency of effective gene insertion is low (of the order of 1 in 10^4 cells or less) and therefore requires the use of large numbers of cells in order to establish cell lines with any regularity. Third, effective integration of the genetic element requires the induction of cell division in tissue culture. Fourth, extended growth in tissue culture is required before cells can be used in experimentation, and this growth usually involves a period of time in artificial conditions which impose highly artificial selective pressure on cell populations.
>
> It would be of great value to have a method which would allow cell lines to be established from a wide variety of cell types with an efficiency and reliability greater than that available with present technology.

In view of this teaching, the skilled artisan would be motivated to use the transgenic animal disclosed therein to establish retinal endothelial and epithelial cell lines rather than the

transfection method of Greenwood *et al.* in order to avoid the disadvantages described by Jat *et al.*

Finally, as discussed above, Jat *et al.* identifies 33 °C as the permissive temperature for expression of the tsA58 transformed phenotype in the various cell lines established from the mouse disclosed therein (see, *e.g.*, column 14, lines 21 and 35; column 18, lines 14, 27, 35 and 44; column 19, line 14; column 22, line 20; column 23, line 64; column 5, line 57; and column 29, line 9). These teachings provide direction and reasonable expectation of success, and one would be motivated to grow the cultures at 33 °C in order to immortalize the cells, which is the nature of the problem solved in the method of Jat *et al.*

Thus, the teachings of Greenwood *et al.* in view of Jat *et al.* provide both direction and motivation to establish cultures of conditionally immortalized retinal epithelial and endothelial cells according to the limitations of the instant claims 5 and 9, which cultures would have the properties of the retinal epithelial and endothelial cells of claims 1-4, 6, 7, 8, 10. Further, in view of the teaching from Greenwood *et al.* that retinal and brain vascular endothelial cells are believed to be identical, the skilled artisan would understand that the retinal endothelial established by the method of Greenwood *et al.* in view of Jat *et al.* would be the same as the brain endothelial cells of the instant claims 11, 12 and 14.

For these reasons, the invention of claims 1-12 and 14, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103 as obvious over the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636